

Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejects claims 40-44 and 69-74 under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Office Action, page 2, section 4.

Specifically, the Examiner alleges that claims 40-44, 69-71, and 73 are indefinite for being incomplete in claims 40 and 69 for omitting essential elements. The Examiner further alleges that "[t]he omitted elements are method steps which indicate how the claimed method operates to enhance a nucleic acid polymerase reaction as disclosed in the specification at the Examples." Office Action, page 3, section 4a.

The Examiner is essentially alleging that claims 40 and 69 must state how (in the case of claim 40) adding a polymerase enhancing composition to a nucleic acid sequence template and at least one nucleic acid polymerase actually enhance a nucleic acid polymerase reaction. Applicants respectfully assert that how a method works need not be part of a claim. The steps of "a) mixing a nucleic acid sequence template for a nucleic acid polymerase with at least one nucleic acid polymerase" and "b) adding a polymerase enhancing composition" are sufficient to carry out the claimed method. Describing exactly how the polymerase enhancing composition works at a molecular level is not necessary to carry out the claimed method.

The Examiner states that "[m]ethod claims need not recite all operating details but should at least recite positive active steps so that the claims will set out ... what subject matter the claims encompass ..." *Id.* Mixing the nucleic acid sequence template and at least one nucleic acid polymerase, and adding a polymerase enhancing composition of the claim are the positive active steps necessary to carry out the claimed method in claim 40. "[H]ow the claimed method operates to enhance a nucleic acid

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polymerase reaction" is not an actual positive step that one performs to practice the claimed method. Applicants respectfully assert that there are no omitted steps in claims 40 or 69.

The Examiner alleges that claims 40-44 are "confusing and redundant in claim 40 at step (a) for [recitation of] 'mixing a nucleic acid sequence template for a nucleic acid polymerase with at least one nucleic acid polymerase.'" Office Action, page 3, section 4b.

Applicants respectfully assert that the meaning of the language is quite clear. The claimed method recites mixing a "nucleic acid sequence template" with a "polymerase." There are many different types of nucleic acid template. The template referred to in claim 40 is a template "for a nucleic acid polymerase." The claimed method allows for more than one polymerase to be mixed, but specifies that the polymerase be a "nucleic acid polymerase." Thus, the language of the claim, to accurately describe the claimed method, is "mixing a nucleic acid sequence template for a nucleic acid polymerase with at least one nucleic acid polymerase."

The Examiner suggestion of inserting the word "reaction" after "template for a nucleic acid polymerase" is appreciated. However, Applicants respectfully point out that this suggestion would change the scope of the claim and be an inaccurate description of the claimed method. A "reaction" implies that a chemical or molecular activity is taking place. There is no reaction until the "at least one nucleic acid polymerase" is mixed with the "nucleic acid sequence template for a nucleic acid polymerase." Thus, it would not make sense to add "at least one nucleic acid polymerase" to a reaction that was already occurring. Applicants respectfully assert that claim 40 is clear and definite.

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The Examiner alleges that claims 43 and 70-74 are indefinite for the recitation of the language "PCR," "RT-PCR," "PEF," and "dUTP." *Id.*, section 4c. The Examiner alleges that abbreviations often have more than one meaning in the art, and suggests that the full names of the abbreviation be recited in the claims.

Applicants respectfully point out that all the abbreviation that the Examiner enumerates are no more ambiguous than the full names the alleged abbreviations stand for. The term "PEF," which stands for polymerase enhancing factor, is fully described and defined, for example, in the specification at page 5, line 32, to page 7, line 33 and page 17, lines 12-24. There is no ambiguity or question that "PEF" stands for anything other than polymerase enhancing factor.

Further, it is well known in the art that the terms "PCR," "RT-PCR," and "dUTP" stand for polymerase chain reaction, reverse transcribed-polymerase chain reaction, and deoxyuridine 5'-triphosphate, respectively. The abbreviations "PCR," "RT-PCR," and "dUTP" are no more ambiguous than the full names. Further, the specification adequately describes PCR, RT-PCR and dUTP, for example, at page 2, line 26 to page 3, line 10; page 42, lines 2-3; and page 63, lines 26-27.

Perhaps, if the Examiner truly believes that, for example, the language "dUTP" is ambiguous, the Examiner could suggest things other than deoxyuridine 5'-triphosphate that one of skill in the art might reasonably mistake the term "dUTP" to stand for.

Applicants respectfully assert that claims 43 and 70-74 are not indefinite.

The Examiner alleges that claims 72 and 74 lack proper antecedent basis for the language "changing the amount of dUTP present or generated during the reaction." *Id.*,

section 4d. The Examiner states that "there is no prior indication that any dUTP was added or generated." *Id.*

During a normal PCR reaction dUTP may be generated by deamination of dCTP, as described in the specification at page 5, lines 9-13. Thus, the generation of dUTP is an inherent property of polymerization reactions. Even if no dUTP is generated, the claim does not necessarily presuppose that any dUTP is added to the reaction. Frequently, dUTP may be found initially in a reaction as a result of template purification.

Claim 72 merely presumes that an amount of dUTP is present in the polymerization reaction, even if that amount is none, and recite "changing the amount of dUTP." Thus, claim 72 and claim 74 are clear and unambiguous.

Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. §112, second paragraph.

#### Rejections Under 35 U.S.C. §102

The Examiner rejects claims 40 and 42-44 under 35 U.S.C. §102(b) as allegedly anticipated by Barnes (*Proc. Nat. Acad. Sci.*, 91:2216-2220, 1994). Office Action, page 4, section 6. Specifically, the Examiner alleges that Barnes teaches the method of claim 40, with a "polymerase enhancing composition comprising an isolated, purified protein obtained from bacteria." *Id.*

Applicants respectfully assert that the Examiner has mischaracterized Barnes. Barnes does not teach a polymerase enhancing composition at all. Barnes merely describes the effects of a combination of polymerases. Applicants assert that adding another polymerase of another type, or more polymerase, is distinct from adding a composition with polymerase enhancing activity. Barnes does not teach a composition

that enhances the activity of a polymerase, but merely teaches adding another polymerase to the polymerase reaction.

Barnes does not anticipate claim 40. Claims 42-44 ultimately depend from claim 40. Thus, for at least the reasons stated above, claims 42-44 are not anticipated by Barnes.

The Examiner rejects claims 40-44 under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Pat. No. 5,449,603 to Nielson et al. ("Nielson"). Office Action, pages 4-5, section 7. Further, the Examiner alleges that Nielson teaches a method of claim 40 with a polymerase enhancing composition comprising a polymerase enhancing protein complex of a naturally occurring protein. *Id.*

Nielson teaches the use of single-stranded nucleic acid binding proteins (SSB) to increase specificity of *hybridization* and decrease nonspecific hybridization. Increasing the specificity of hybridization refers to the hybridization of one strand of a nucleic acid to another, not to enhancing polymerase activity. Nowhere does Nielson teach a method of mixing a nucleic acid sequence template for a nucleic acid polymerase with at least one nucleic acid polymerase; and adding a polymerase enhancing composition.

Applicants respectfully submit that the Examiner has failed to show that Nielson teaches a method of mixing a nucleic acid sequence template for a nucleic acid polymerase with at least one nucleic acid polymerase; and adding a polymerase enhancing composition. Claim 40 is not anticipated by Nielson.

Claims 41-44 ultimately depend from claim 40. Thus, for at least the reasons stated above, claims 41-44 are not anticipated by Nielson.

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The Examiner rejects claims 71 and 73 under 35 U.S.C. §102(a) as allegedly anticipated by Lasken et al. (JBC, 271:17692-17696, 1996) ("Lasken"). The Examiner alleges that Lasken teaches a "method of enhancing a nucleic acid polymerase reaction comprising performing a reaction in the presence of a dUTPase activity." Office Action, page 5, section 7.

Applicants respectfully assert that a careful reading of Lasken does not teach a method of enhancing polymerase activity in the presence of a dUTPase activity. The portions of Lasken cited by the Examiner describe the inhibition of polymerase activity by uracil containing DNA, the incorporation of dUTP into polymerization by an exo- Vent polymerase (Lasken, p.17694, lines 3-10), or the incorporation of dUMP (not dUTP) into polymerization when dTTP and dUTP are absent (Lasken, p.17696, lines 19-21 and 28-31). Nowhere does Lasken describe polymerase enhancement by the presence of dUTPase activity. The Examiner has failed to show where Lasken teaches a method of enhancing polymerase activity in the presence of a dUTPase activity.

Claims 71 is not anticipated by Lasken. Claim 73 depends from claim 71. For at least the reasons stated above, claim 73 is not anticipated by Lasken.

Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. §102.

#### Double Patenting

The Examiner rejects claims 40-44 and 69-74 under the judicially created doctrine of obviousness-type double patenting over claims 1-29 of U.S. Pat. No. 6,183,997 B1. Office Action, pages 6-7, section 9.

Without acquiescing to the rejection, when the Examiner finds the claims are otherwise in a condition for allowance, the Applicants will submit a terminal disclaimer to obviate the double patenting rejection.

Conclusion

Applicants request reconsideration and withdrawal of all rejections. Applicants respectfully submit that claims 40-44 and 69-74 are in condition for allowance.

If there is any fee due in connection with the filing of this Response, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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